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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,341	05/03/2002	Michael R. Hayden	SMAR-0013	8795

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/019,341	HAYDEN ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,37-40 and 42-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,37-40 and 42-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to the Amendment filed 9/18/2008. Claims 35, 37-40 and 42-51 are pending.

Applicants' arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

Election/Restrictions

Applicant elected Group II and the disease hyperlipidemia with traverse in the reply filed on 9/23/2004. Currently, claims 35, 37-40 and 42-51 are under consideration.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 35, 37-40 and 42-51 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,814,962 (hereafter '962) in view of Kozaki et al (Journal of Lipid Research, Vol. 34, pages

1765-1772, 1993, of record; see the entire reference) as evidenced by Gotoda et al (Nucleic Acids Research, Vol. 17, No. 6, page 2351, 1989, of record; see the entire reference). This rejection was made in the Office action mailed 3/18/2008 and is reiterated below.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claims.

In the instant case, claims 1-6 of the '962 patent recite methods of treating dyslipoproteinaemia, hypertriglyceridaemia, hypercholesterolaemia, hyperlipidaemia, familial hypertriglyceridaemia, and combined familial hyperlipidaemia and postprandial hyperlipidaemia comprising administering to the patient a defective recombinant adenovirus comprising a nucleic acid sequence coding for a biologically active human lipoprotein lipase (LPL). The claims of the '962 patent differ from the claims of the instant application in that they fail to disclose the use of a nucleic acid sequence encoding the S447X variant of human LPL.

Kozaki et al teach an expression vector comprising the S447X LPL cDNA sequence (e.g. Figure 2). Further, Kozaki et al demonstrate that the S447X LPL protein has a specific activity about twice as high as wild type LPL (e.g. Figures 3 and 4, LPL-446).

The S447X LPL nucleic acid taught by Kozaki et al necessarily encodes an LPL S447X protein with at least 90% identity to SEQ ID NO: 3 and at least 95% identity to SEQ ID NO: 1. Kozaki et al disclose the primer sequences used to make the S447X truncation in the Figure 2 legend and cite Gotoda et al (Nucleic Acids Research, Vol. 17, No. 6, page 2351, 1989) as the source of the human sequence (e.g. page 1766, Site-directed mutagenesis, see cited reference

22). As demonstrated in the alignment mailed 11/19/2004, the nucleic acid sequence disclosed by Gotoda et al is 100% identical to SEQ ID NO: 3. Because SEQ ID NO: 1 has a c-terminal truncation of 2 amino acids relative to SEQ ID NO: 3, the nucleic acid sequence disclosed by Gotoda et al is capable of producing an alignment with 100% identity over the entire length of SEQ ID NO: 1.

Therefore, it would have been obvious to modify the method of claims 1-6 of the '962 patent to include the S447X nucleic acid sequence taught by Kozaki et al because the claims recite the use of a nucleic acid encoding a biologically active human LPL and Kozaki et al teach that the S447X truncation is a functional LPL protein. One would have been motivated to make such a modification in order to receive the expected benefit of increased LPL activity as taught by Kozaki et al.

Response to Arguments - Double Patenting

With respect to the rejection of claims 35, 37-40 and 42-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,814,962, Applicant's arguments filed 9/18/2008 have been fully considered but they are not persuasive.

The response notes that the teachings of Kozaki et al must be viewed in the context of additional references. The response notes that Kozaki et al state that contradictory results have been published concerning the effect of the S447X truncation on LPL activity. Kozaki et al specifically refer to reference 10 (Faustinella et al) reporting that the S447X truncation has no effect on LPL activity in vitro, i.e., neither an increase nor decrease of activity as compared to

wt-LPL. The response notes that Faustinella et al further report that "the Ser^{447} -> Ter mutation…is a sequence polymorphism of no functional significance." Kozaki et al specifically refer to reference 29 (Kobayashi et al), which reports that the S447X truncation when expressed in vitro results in a reduction of LPL activity that is 45% of wt-LPL. The response notes that Kobayashi et al suggest that the truncation is pathological, in the sense that it is suggested that it might be "responsible for the property of the LPL with a defect in lipid interface recognition in the type I patient. The response notes that in the face of this contradictory evidence, Kozaki et al end the paragraph at page 1771 with the conclusion "[b]ut further studies are required to show the effect of the Ser447 stop mutation."

These arguments are not found persuasive. The teachings of Kozaki et al must be viewed in the context of additional references that demonstrate the state of the art at the time the invention was made. The specification states the following with respect to the correlation between the S447X mutation and the level of HDL-C:

> A mutation that introduces a termination codon at position 447 in place of a serine codon (Ser447Ter or S447X) has been associated with decreased TG and **increased HDL-cholesterol levels** (Hokanson, 1997, International Journal of Clinical and Laboratory Research 27, 24-34; Gagne et al,. *Arterioscl. Thmmb.* 1994, 14(8):1250-1257; Mattu et al., 1994, Arteriosclerosis and Thrombosis 14, 1090-1 097; Kuivenhoven et al., 1997, Arteriosclerosis, Thrombosis and Vascular Biology 17, 595-599; Groenemeijer et al., 1997, Circulation 95, 2628-2635; Fisher et al., 1997, Atherosclerosis 135, 145-159; U.S. Patent No. 5,658.729; Groenemeijer et al., Circulation 1997, 95:2628-2635; Gagne et al., *Clin.Genet.* 1999, 55(6):450-454). Correspondingly, in **most** studies this mutation seems to confer protection against CAD. The mechanism(s) behind these effects are not known. (emphasis added)

The cited references have been made of record on IDS filed 9/30/2002. Consideration of the evidence on the record as a whole shows that the ability of LPL to increase HDL-C is more likely than not.

The response asserts that the present application provides surprising results from animal models. The response specifically points to Example 1, which is asserted as establishing that LPL was not effective to treat the mouse model of complete LPL deficiency, whereas the LPL-S447X variant was effective. The response notes that this is particularly relevant for claim 37. Further, the response points to Examples 2 and 5 of the specification, which are asserted to show a dramatic difference between treatment with wt LPL and treatment with LPL-S447X in mouse models that do not have complete LPL deficiency: +/- LPL in Example 2 and -/- ApoE in Example 5. In Example 2, the response notes that there was a significant increase in both HDL-C and total-C only in the Ad-447 group. At the same dose, in the Ad-LPL cohort, there was a slight decrease in HDL-C. Thus, the response asserts that there is no teaching in the cited references upon which one skilled in the art could form a reasonable expectation of success in using a viral vector to deliver an amount of S447X therapeutic effective to lower triglycerides and to raise HDL-C in patients suffering from hyperlipidemia associated with LPL or ApoE deficiency.

These arguments are not found persuasive. In Example 1, the specification does not disclose the dosage and specific administration of Ad-LPL. Thus, it is not clear that Ad-LPL is incapable of rescuing LPL deficient mice. Weinstock et al (J. Clin. Invest., Vol. 96, pages 2555-2568, 1995, cited as reference 125 on the IDS filed 9/30/2002) teaches that LPL deficient mice can be rescued by breeding a transgenic line containing the mouse muscle creatine kinase promoter driving a human LPL minigene onto the LPL knockout background (e.g., page 2559, right column, last paragraph). Muscle-specific expression of human LPL rescued the LPL knockout mice, allowing them to survive into adulthood, at which time they had a normal

lipoprotein profile (e.g., page 2559, right column, last paragraph; Figure 8). Treatment of the knockout mice with human LPL resulted in an increase in HDL-C as compared to the knockout mice not treated with human LPL (e.g., Figure 8). Further, Weinstock et al teach that several groups have made LPL transgenic mice and found that LPL overexpression causes **decreased triglycerides** and **increased HDL** (e.g., page 2555, right column). Thus, the expectation would be that treatment with a gene therapy vector encoding an active LPL protein would result in a decrease in triglycerides and an increase in HDL-C. The teaching in the specification that Ad-LPL caused a **decrease in HDL-C** in LPL deficient mice is unexpected. The finding that Ad-447 caused an increase in HDL-C is expected based upon the teachings of the prior art. The claims are drawn to a method where LPL S447X protein is expressed from a gene therapy vector to lower triglycerides and raise HDL-C. The finding that Ad-447 encoding the LPL S447X protein results in decreased triglycerides and increased HDL is consistent with the teachings in the prior art and is expected. Kozaki et al teach that the LPL-446 (LPL S447X) protein has LPL activity. Thus, it is expected that treatment with LPL S447X protein results in decreased triglycerides and increased HDL-C. The claims are not drawn to decreasing HDL-C by administering Ad-LPL to a subject with homozygous LPL deficiency, which would be unexpected. Furthermore, the specification does not teach that Ad-LPL causes a reduction in HDL-C in an ApoE knockout mouse (e.g., Table 2 on page 32). The post-heparin plasma levels of HDL-C (mg/dl) are 12 ± 1 for control, 14 for Ad-447 and 13 ± 4 for Ad-LPL.

Considering the evidence as a whole, the replacement of the LPL sequence of the '962 patent with the LPL S447X sequence of Kozaki et al would have been obvious to one of ordinary

skill in the art at the time the invention was made for the reasons set forth above, and the reasons made of record in the previous office actions. Thus, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 35, 37-40 and 42-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayden et al (WO 96/11276, of record; see the entire reference) in view of Kozaki et al (Journal of Lipid Research, Vol. 34, pages 1765-1772, 1993, of record; see the entire reference) as evidenced by Gotoda et al (Nucleic Acids Research, Vol. 17, No. 6, page 2351, 1989; see the entire reference). This rejection was made in the Office action mailed 3/18/2008 and is reiterated below.

Hayden et al teach the *in vivo* transduction of human cells with viral gene therapy vectors comprising the full-length LPL cDNA sequence for the treatment of hypertriglyceridemia (i.e. one form of hyperlipidemia) resulting from heterozygous or homozygous LPL deficiency (e.g. page 11, lines 10-31; page 12, lines 1-31). Hayden et al teach that decreased catalytic activity of lipoprotein lipase in humans results in lower HDL-C levels and higher triglyceride levels (e.g., page 2, lines 15-22; Example 1). Further, Hayden et al teach that gene therapy to introduce functional LPL may reduce the clinical manifestations stemming from hypertriglyceridemia

(e.g., page 11, lines 10-16). Hayden et al teach the use of viral gene therapy vectors such as adenovirus (e.g., page 11, lines 10-16; page 12, lines 6-9 and 25-31).

Hayden et al do not teach the administration of a S447X LPL cDNA sequence.

Kozaki et al teach an expression vector comprising the S447X LPL cDNA sequence (e.g. Figure 2). Further, Kozaki et al demonstrate that the S447X LPL protein has a specific activity about twice as high as wild type LPL (e.g. Figures 3 and 4, LPL-446). Moreover, Kozaki et al suggest that the S447X mutation may have some protective effect against the development of hypertriglyceridemia (e.g. page 1771, left column, paragraph 1).

The S447X LPL nucleic acid taught by Kozaki et al necessarily encodes an LPL S447X RNA with at least 90% identity to nucleotides 256 through 1599 of SEQ ID NO: 4 and encodes a protein with at least 90% identity to SEQ ID NO: 3 and at least 95% identity to SEQ ID NO: 1. Kozaki et al disclose the primer sequences used to make the S447X truncation in the Figure 2 legend and cite Gotoda et al (Nucleic Acids Research, Vol. 17, No. 6, page 2351, 1989) as the source of the human sequence (e.g. page 1766, Site-directed mutagenesis, see cited reference 22). As demonstrated in the alignment mailed 11/19/2004, the nucleic acid sequence disclosed by Gotoda et al is 100% identical to SEQ ID NO: 3. Because SEQ ID NO: 1 has a c-terminal truncation of 2 amino acids relative to SEQ ID NO: 3, the nucleic acid sequence disclosed by Gotoda et al is capable of producing an alignment with 100% identity over the entire length of SEQ ID NO: 1.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the adenoviral gene therapy vector of Hayden et al to include the S447X nucleic acid sequence taught by Kozaki et al in place of the wild type LPL sequence because

Hayden et al teach it is within the ordinary skill in the art to use an LPL coding sequence in the adenoviral gene therapy vector for the treatment of hyperlipidemia associated with LPL deficiency and Kozaki et al teach that the S447X truncation is a functional LPL protein.

One would have been motivated to make such a modification in order to receive the expected benefit of increased LPL activity and a protective effect against the development of hypertriglyceridemia as taught by Kozaki et al. Since Hayden et al teach that decreased activity of LPL results in higher triglycerides and lower HDL-C, one would expect that increasing the LPL activity in a human would result in lower triglycerides and higher HDL-C. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

With respect to the rejection of claims 35, 37-40 and 42-51 under 35 U.S.C. 103(a) as being unpatentable over Hayden et al in view of Kozaki et al, as evidenced by Gotoda et al, Applicant's arguments filed 9/18/2008 have been fully considered but they are not persuasive.

The response notes that the teachings of Kozaki et al must be viewed in the context of additional references. The response notes that Kozaki et al state that contradictory results have been published concerning the effect of the S447X truncation on LPL activity. Kozaki et al specifically refer to reference 10 (Faustinella et al) reporting that the S447X truncation has no effect on LPL activity in vitro, i.e., neither an increase nor decrease of activity as compared to wt-LPL. The response notes that Faustinella et al further report that "the Ser^{447} -> Ter

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> A mutation that introduces a termination codon at position 447 in place of a serine codon (Ser447Ter or S447X) has been associated with decreased TG and **increased HDL-cholesterol levels** (Hokanson, 1997, International Journal of Clinical and Laboratory Research 27, 24-34; Gagne et al,. *Arterioscl. Thmmb.* 1994, 14(8):1250-1257; Mattu et al., 1994, Arteriosclerosis and Thrombosis 14, 1090-1 097; Kuivenhoven et al., 1997, Arteriosclerosis, Thrombosis and Vascular Biology 17, 595-599; Groenemeijer et al., 1997, Circulation 95, 2628-2635; Fisher et al., 1997, Atherosclerosis 135, 145-159; U.S. Patent No. 5,658.729; Groenemeijer et al., Circulation 1997, 95:2628-2635; Gagne et al., *Clin.Genet.* 1999, 55(6):450-454). Correspondingly, in **most** studies this mutation seems to confer protection against CAD. The mechanism(s) behind these effects are not known. (emphasis added)

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The response asserts that the present application provides surprising results from animal models. The response specifically points to Example 1, which is asserted as establishing that LPL was not effective to treat the mouse model of complete LPL deficiency, whereas the LPL-S447X variant was effective. The response notes that this is particularly relevant for claim 37. Further, the response points to Examples 2 and 5 of the specification, which are asserted to show a dramatic difference between treatment with wt LPL and treatment with LPL-S447X in mouse models that do not have complete LPL deficiency: +/- LPL in Example 2 and -/- ApoE in Example 5. In Example 2, the response notes that there was a significant increase in both HDL-C and total-C only in the Ad-447 group. At the same dose, in the Ad-LPL cohort, there was a slight decrease in HDL-C. Thus, the response asserts that there is no teaching in the cited references upon which one skilled in the art could form a reasonable expectation of success in using a viral vector to deliver an amount of S447X therapeutic effective to lower triglycerides and to raise HDL-C in patients suffering from hyperlipidemia associated with LPL or ApoE deficiency.

These arguments are not found persuasive. In Example 1, the specification does not disclose the dosage and specific administration of Ad-LPL. Thus, it is not clear that Ad-LPL is incapable of rescuing LPL deficient mice. Weinstock et al (J. Clin. Invest., Vol. 96, pages 2555-2568, 1995, cited as reference 125 on the IDS filed 9/30/2002) teaches that LPL deficient mice can be rescued by breeding a transgenic line containing the mouse muscle creatine kinase promoter driving a human LPL minigene onto the LPL knockout background (e.g., page 2559, right column, last paragraph). Muscle-specific expression of human LPL rescued the LPL knockout mice, allowing them to survive into adulthood, at which time they had a normal

lipoprotein profile (e.g., page 2559, right column, last paragraph; Figure 8). Treatment of the knockout mice with human LPL resulted in an increase in HDL-C as compared to the knockout mice not treated with human LPL (e.g., Figure 8). Further, Weinstock et al teach that **several groups** have made LPL transgenic mice and found that LPL overexpression causes **decreased triglycerides** and **increased HDL** (e.g., page 2555, right column). Thus, the expectation would be that treatment with a gene therapy vector encoding an active LPL protein would result in a decrease in triglycerides and an increase in HDL-C. The teaching in the specification that Ad-LPL caused a **decrease in HDL-C** in LPL deficient mice is unexpected. The finding that Ad-447 caused an increase in HDL-C is expected based upon the teachings of the prior art. The claims are drawn to a method where LPL S447X protein is expressed from a gene therapy vector to lower triglycerides and raise HDL-C. The finding that Ad-447 encoding the LPL S447X protein results in decreased triglycerides and increased HDL-C is consistent with the teachings in the prior art and is expected. Kozaki et al teach that the LPL-446 (LPL S447X) protein has LPL activity. Thus, it is expected that treatment with LPL S447X protein would result in decreased triglycerides and increased HDL-C. The claims are not drawn to decreasing HDL-C by administering Ad-LPL to a subject with homozygous LPL deficiency, which would be unexpected. Furthermore, the specification does not teach that Ad-LPL causes a reduction in HDL-C in an ApoE knockout mouse (e.g., Table 2 on page 32). The post-heparin plasma levels of HDL-C (mg/dl) are 12 ± 1 for control, 14 for Ad-447 and 13 ± 4 for Ad-LPL.

Considering the evidence as a whole, the replacement of the LPL sequence of Hayden et al with the LPL S447X sequence of Kozaki et al would have been obvious to one of ordinary

skill in the art at the time the invention was made for the reasons set forth above, and the reasons made of record in the previous office actions. Thus, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

/Celine X Qian /
Primary Examiner, Art Unit 1636